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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,721	09/22/2003	Angela M. Belcher	027053-0107	5505

23533 7590 01/17/2007

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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	**PAPER NUMBER**
1639	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/665,721	BELCHER ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *144,147-156,158 and 159* is/are pending in the application.

4a) Of the above claim(s) *154-156 and 159* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *144,147-153 and 158* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/20/2006 has been entered.

Status of Claims

Claims 144, 147-156 and 158-159 are pending.

Claims 154-156 and 159 are withdrawn from consideration.

Claims 144, 147-153 and 158 are under consideration.

Withdrawn Objection and Rejection

In view of the amendments to the claims, the 132 declaration of Belcher and applicants' arguments, the 35 USC 112, first paragraph, written description is withdrawn. Also, the 35 USC 102 rejection over the Lawton, Josephson et al, Mattoussi et al, Brown et al and Mayes et al references and 35 USC 103 rejection over Sakaguchi et al are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 144, 147-153 and 158, as amended, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (This is a new matter rejection).

The as-filed specification does not provide support for an "isolated" peptide and "preselected" metal nanoparticle, within the context of the claimed invention. Also, "***up*** to 20 amino acids" would read on zero as the lower limit. MPEP 714.02 recites that applicants specifically point out where in the specification support for the new claimed limitations specifically appear.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 144, 147-153 and 158, as amended, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 144 drawn to a composition comprising a "pre-selected" metal nanoparticle is indefinite. It is not clear whether the metal should first be preselected and then bound to an isolated peptide to form a composition or the metal bound to the peptide had already been selected? A claim to a composition should contain a definite compound/component and not a mere probability that it can contain the component. The claim composition appears to be drawn to a method (in the pretext of a composition) as it recites the manipulative step of preselecting and selecting binding. Furthermore, the claim composition of a "preselected metal ***bound*** to an isolated peptide" appears contradictory to the claimed "isolated peptides ..which ***selectively binds*** to the pre-selected metal nanoparticle". If it is already preselected, is there a chance it would not

selectively bind to the peptide? Pre-selection does not recite a positive definition of a compound contain in a composition.

2. In claim 147, is "selectively nucleates the metal" different from the "selectively bind to the preselected metal" recited in the independent claim 144?

3. The inconsistent use of the terms "nanoparticle" (claim 149); "metal nanoparticles" (claims 147 and 148); "the metal alloy" in e.g., claim 151 provides for confusion and ambiguity. Cf. with the recitation of a preselected metal nanoparticles in the base claim 144.

Double Patenting

Claim 144, for example, is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 37, for example of copending Application No. 10/157,775 ('775 application) or claim e.g., 78 0f copending application 10/155,883 ('883 application) or of claims e.g., 52, 63 and 64, of copending Application No. 10/158,596 ('596). This is a provisional double patenting rejection since the conflicting claims have not in fact been patented and reiterated below. [Note due to the excessive number of claims only the base claim in each applications are cited in the rejection.]

Each of the applications is drawn to nearly identical composition. The instant invention claims a metal binding

molecule-synthesized metal particles which is nearly identical to the composition of e.g., '775 application. The '775 application directly recites a composition comprising a metal and binding molecule, as the bacteriophage library. Although each of the claims is worded differently, however, as evident from each of these applications' disclosure the same composition i.e., library of phage and metal is disclosed and described in all of the copending applications.

Response to Arguments

Applicants will address these provisional grounds of rejection, if one of the applications used to make the provisional rejection issues into a patent before allowance of the present application.

In reply, since applicants have not set a clear demarcation line among these applications, the double patenting rejection is maintained.

Double Patenting (Obviousness-type)

Claim 144, for example, is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 37 of copending Application No. 10/1557,775 or claim 78, for example, of copending application

No. 10/155,883 or of claims e.g., 52, 63 and 64, inter alia, of copending Application No. 10/158,596. Although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons stated above under the 101 double patenting rejection. Furthermore, the form assumes by each of the different compositions do not make the composition different from one another as the compounds in the composition is the same. To make a composition in different forms would be an obvious design choice.

The response above is incorporated herein.

In the absence of a terminal disclaimer, the obviousness double patenting rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 144, 147-153 and 158, as amended, are rejected under 35 U.S.C. 102(b) as being anticipated by Kresse et al (6,048,515), as reiterated below.

Kresse discloses at e.g., col. 15, line 3 up to col. 16, line 61, including Table 2 and the claims at col. 37, a composition comprising peptides that have an affinity for the iron core (nanoparticle metal, as claimed). The preferred peptides contain the RRTVKHHVN or RRSRHH or RSKRGR sequence or parts thereof in their molecule [one-letter code of amino acids). The peptides have been selected from peptide libraries using biochemical methods.

Accordingly, the specific compositions of Kresse containing the specific metal components and synthetic peptides fully meet the claimed composition comprising broadly a nanoparticle metal and isolated peptides of undefined structure.

Response to Arguments

Applicants acknowledge that Kresse teaches a nanoparticle comprising an iron core, a synthetic polymer primary coating over the iron core, and a secondary coating over the primary coating. Kresse, abstract. In some embodiments, an "adsorption mediator/enhancer," such as a peptide, can be used to facilitate coating the iron core with the primary coating. Kresse at col. 5, 11.22-24. Kresse further discloses that the peptides

preferably have an "affinity" for the iron core and that these peptides "can be selected from peptide libraries using advanced biochemical methods." Kresse at col. 15, 11. 14-20. But argue that the quotation is nothing more than a wish or a plan for how one might begin to try to obtain a peptide with affinity for iron. Without any enabling disclosure of a particular library or the conditions used to prepare the iron for use with the library, the reference cannot anticipate or render obvious the presently claimed invention.

In response, it is not clear how the Kresse reference which recites a peptide library from which the specific peptides are isolated and the specific metal to which the peptides have affinity can be non-enabling. While on the other hand, Applicants' composition drawn to a generic preselected metal and a peptide of no defined structure reciting only the length of the peptide is enabled.

Applicants argue that there is no evidence that Kresse's peptides are capable of selectively binding to iron. The closest that Kresse comes is to state that certain peptides obtained by unidentified "advanced" biochemical methods have "affinity" for iron. It is important to recognize that a peptide having affinity for iron is not necessarily a peptide that selectively

binds to iron. The present specification explains selective binding in paragraph 119, using a Co-binding peptide as an example, in the following manner (underlining supplied):

[0119] Additionally, the Co-specific phage was exposed to several different material surfaces. The results are depicted in FIG. 6. The Co-specific phage possessed a relative higher affinity for Co than either the wild-type phage or a random phage library sequence (FIG. 6A). Additionally, the Co-specific phage displayed a greater affinity for Co than for Si, suggesting they bound preferentially to the Co surface. Having affinity for iron does not mean that Kresse's peptides are selective for iron over other materials.

In reply, the fact that Kresse discloses that the iron metal alloy is primarily coated with a peptide obtained from a library indicates that it selectively binds to only metal iron alloy with high affinity. As indicated in the instant specification at paragraph 119, ***greater affinity*** of Co-specific page displayed for CO than for Si equates affinity for selectivity binding. Silence in the prior art teaching does not indicate that the prior art did not do what applicants did. The fact that Kresse indicates the high affinity binding would have indicated the relative affinity of the metal iron to the other metals present therein.

Applicants state that unlike the present specification, Kresse provides no evidence that the peptides would selectively bind to iron. In fact, Dr. Belcher explains in her accompanying Declaration that the sequences of the Kresse peptides appear to be similar to universal binding peptides that are non-selective for a specific metal. The specific peptides listed in Kresse are: "RRTVKHHVN or RRSRHH or RSKRGR sequence". These have a high degree of similarity to the non-selective sequences, as explained in Dr. Belcher's Declaration. Thus, the available evidence suggests it is more likely than not that Kresse's peptides are not selectively binding peptides. This is consistent with the overall context of the Kresse invention, which does not need selectively binding peptides based on the way in which the peptides are used and which does not describe a methodology that would lead to a selectively binding peptides.

In reply, the arguments that Kresse does not describe a methodology that would lead to a selectively binding peptides are not commensurate in scope with the claims. This is also true for declarant's statement at paragraphs 4 and 5 of the 132 declaration. Furthermore, declarant's comparison of the Kresse's specific peptides of defined structure with the universal non-binding peptides is unclear. The claimed composition does not contain any peptide structures, which could possibly fall also

into a universal non-selective binding. See paragraph 119 above which recites that selectively occurs only for Co-specific phage not even for a random phage or the specific wild type phage. Note further that the universal binders differ from Kresse's compounds not only in the amino acid contained therein but also in the length of the peptides. It is not apparent from the universal binders the location of the residue where selective binding occurs. There is nothing in the claims that preclude that Kresse's peptide are not selective binders, as the claims do not recite for any selectively binding peptides to be specific for a specific metal.

Claims 144-147, as amended, are rejected under 35 U.S.C. 102(a) as being anticipated by Lee et al (Science).

The claimed composition comprising broadly a nanoparticle metal and synthetic peptides of undefined structure is fully met by the specific composition of Lee comprising of ZnS and phage or a peptide with ZnS as disclosed at e.g., page 892, col.2 up to page 895, col. 3 and Example 4, number 7.

Response to Arguments

Applicants state that Lee discloses the formation of semiconductor (ZnS) nanocrystals using genetically engineered M13 bacteriophage. Metals have very different properties

compared to the ionic solids that are disclosed in Lee. For example, ionic solids have surfaces that are charged or have alternating charged atoms. One of skill in the art would expect that peptides would be more selective to such solids, because peptides also often have regions of alternating charge. Metals, on the other hand, have different electronegativities (covalent rather than ionic). Thus, obtaining selectivity for different metals using peptides would not be expected based on the teachings of Lee. Accordingly, Lee does not teach or suggest the claimed invention to the skilled artisan. Furthermore, Lee in no way suggests that a peptide could be created that is capable of nucleating metal nanoparticles from solution. For this reason, claim 147 should not be subject to this rejection. As explained at the interview, it was a surprising discovery that the peptides of the present invention could nucleate metal nanoparticles from solution at room temperature.

In reply, there is nothing in the claims to preclude the metal crystals of Lee from the instant metal i.e., that the instant metal are covalently binding metals or is strictly defined as argued. Attention is drawn to Lee's disclosure page 892, col. 2 which recites nucleation of metals.

Claims 144, 1448, 150, 152 and 158, as amended, are rejected under 35 U.S.C. 102(a) as being anticipated by Whaley et al (Nature).

Whaley et al discloses at page 665, cols. 1 and 2 a composition comprising of combinatorial phage-display libraries comprising of peptides that bind to a range of crystalline semiconductor surfaces such as Gas, GaAs, and Si, inter alia. The peptide binding sequences comprised in the phage display libraries each contain 12 amino acids fused to pIII coat protein of MI3.

Claims 144, 1448, 150, 152 and 158, as amended, are rejected under 35 U.S.C. 102(b) as being anticipated by Torres-Martinez(Nanotechnology).

Torres-Martinez discloses at pages 340-349 a composition comprising of a glutathione peptides that cap or binds ZnS nanocrystals.

Claims 144, 1448, 150, 152 and 158, as amended, are rejected under 35 U.S.C. 102(b) as being anticipated by Service (Science).

Service discloses at page 2443 up to page 2444 a composition comprising ZnS and GaAs and a peptide comprised in a bacteriophage virus.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 144, 147-153 and 158,a s amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over Mayes et al (USP 6713173) in view of either Brown et al (Nature Biotechnology) or Whaley et al.

Mayes discloses at e.g., claims 3-6:

> 1. A data storage medium (composition, as claimed)comprising a magnetizable layer, wherein said magnetizable layer comprises a plurality of at least partially encased ferromagnetic particles comprising a metal or metal alloy, wherein each of said ferromagnetic particles has been formed and is at least partially encased within the cavity of one of a protein or protein macromolecule, wherein said cavity of said protein or protein macromolecule is of a uniform predetermined size and shape.
>
> 2. The medium according to claim 1, wherein the protein is apoferritin.
>
> 3. The data storage according to claim 1 comprising ferromagnetic particles elected from the group of metals consisting of: cobalt, platinum, iron, and nickel.
>
> 4. The data storage medium according to claim 3, wherein the ferromagnetic particles are cobalt metal particles.
>
> 5. The data storage medium according to claim 1, wherein the ferromagnetic particles comprise an alloy of two or more metals selected from the group consisting of: aluminium, barium, bismuth,

cerium, chromium, cobalt, copper, iron, manganese, molybdenum, neodymium, nickel, niobium, platinum, praseodymium, samarium, strontium, titanium, vanadium, ytterbium, and yttrium.

6. The data storage medium according to claim 5, wherein the ferromagnetic particles are ferromagnetic metal alloy particles selected from the group of metal alloys consisting of: an alloy of cobalt and platinum; an alloy of cobalt, platinum and chromium; an alloy of iron and platinum; an alloy of manganese and aluminum; and alloy of samarium and cobalt; and an alloy of neodymium and iron.

Mayes does not disclose a peptide as claimed in the composition. However, Brown discloses at page 269, col. 1:

Understanding the mechanisms by which proteins recognize surface features is a central goal in biology. Metal surfaces provide a model system to study surface recognition by proteins. One genetic approach used to analyze the recognition properties of proteins is peptide display. ***In these approaches, large populations of random peptides are displayed on the surface of either beads, bacteriophage, or bacteria in such a way that each particle displays peptides of a single amino acid sequence.*** The population of particles are exposed to the target surface and those that recognize the surface and adhere are recovered and analyzed. Short peptides, however, can often attain multiple conformations, reducing the concentration of the active form. The polypeptides produced would be large enough to encode their own folding information while retaining a low complexity. Low complexity should aid in analyses leading to modeling and eventual manipulation of the structure of the folded polypeptide. Large populations of repeating polypeptides have been constructed and repeating polypeptides that were able to adhere avidly to, and distinguish, metal surfaces were isolated.

Whaley discloses at page 666, col. 1:

To help elucidate the exact binding sequence, we have begun screening our surfaces with shorter libraries, including 7-mer and disulphide constrained 7-mer libraries. By reducing the size and flexibility of the binding domain, fewer peptide--surface interactions are allowed, thereby increasing the strength of interactions between generations of selection.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to substitute the protein in the composition of Mayes with a shorter length peptide as taught by Brown. The advantage in the used of peptide isolated from bacteriophage taught by Brown or Whaley, supra would provide the motivation to one skill in the art to use a short peptide in metal surface recognition for the peptide.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571) 272-0763 The fax phone number for the organization where this application or proceeding is assigned is 571 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
January 4, 2007